Egyptian Pediatric Association Gazette (2015) **63**, 69–73

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Egyptian Pediatric Association Gazette

journal homepage: http://www.elsevier.com/locate/epag

CASE REPORT

Hashimoto's encephalopathy presenting with acute confusional state in a patient with hypothyroidism

Naglaa Fathy Barseem [a,*], **Mohamed Ahmed Helwa** [b]

[a] *Pediatric Department, Faculty of Medicine, Menoufia University, Egypt*
[b] *Department of Clinical Pathology, Faculty of Medicine, Menoufia University, Egypt*

Received 24 October 2014; revised 27 March 2015; accepted 16 April 2015
Available online 8 May 2015

KEYWORDS

Hashimoto's encephalopathy;
Autoimmune thyroid disease-children

Abstract Hashimoto's encephalopathy is a neurological disorder of unknown etiology associated with thyroid autoimmunity. The disease may present as two types, a sudden vasculitic type or a progressive subacute type associated with cognitive dysfunction, confusion and memory loss.
We report a case of a 6 year old previously healthy Egyptian female , who developed a subacute onset of declining upper brain function. Serologic studies demonstrated high levels of antithyroid antibodies. Electroencephalographic and magnetic resonance image findings were consistent with Hashimoto's encephalopathy.
Hashimoto's encephalopathy is a diagnosis of exclusion. This unusual disorder is often underrecognized because of multiple neurocognitive manifestations; therefore, it is important to be aware of the clinical manifestations to make a correct diagnosis.

Introduction

Hashimoto's encephalopathy (HE) is a rare condition associated with Hashimoto's disease. Hashimoto's thyroiditis (HT) is a common form of chronic autoimmune thyroid diseases.[1] The cause of HE has been proposed to be autoimmune because of its association with other immunologic disorders (myasthenia gravis, glomerulonephritis, primary biliary cirrhosis, pernicious anemia and rheumatoid arthritis), female predominance, inflammatory findings in the cerebrospinal fluid (CSF) and response to treatment with steroids.[2,3] HE consists of two sub types. The first is an insidious, recurrent vasculitic type, demonstrating stroke-like attacks concomitant with impairment of consciousness, and the second is progressive and the more commonly seen form of encephalopathy, which presents itself with confusion, psychosis, somnolence and coma.[4,5] The underlying mechanism in both HE and HT is autoimmunity. Two possible mechanisms were suggested in the development of HE. The first of these might be the result of edema and reduction in the vasculature due to autoimmune mediated central nervous system vasculitis together with impairment of the microvascular structure. The other is the formation of antineural antibodies and cross-reaction due to a common antigen of both the thyroid gland and the brain.[6]

* Corresponding author. Tel.: +20 1000314897.
E-mail address: naglaa_b2000@yahoo.com (N.F. Barseem).
Peer review under responsibility of Egyptian Pediatric Association Gazette.

http://dx.doi.org/10.1016/j.epag.2015.04.002

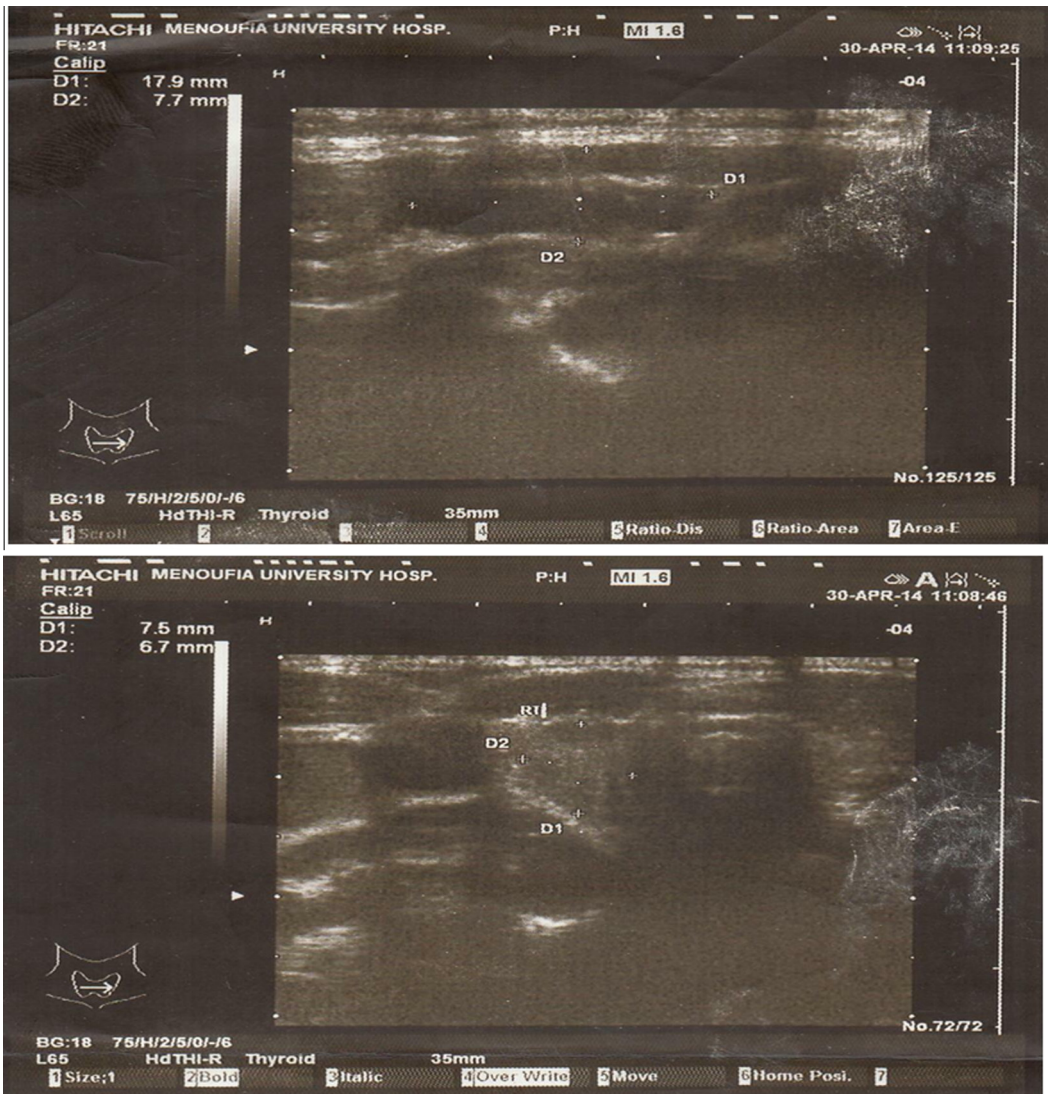

Figure 1 U/S on the thyroid gland showed a picture of chronic thyroiditis (hypoechogenic lobes).

Case presentation

A six year old Egyptian female child fourth in order out of five off spring, of positive consanguinity was admitted to the hospital complaining of hypo activity (her level of functioning prior to illness had been adequate, subsequently returning to a similar level after recovery from episodes) and changed sensorium (changes in level of consciousness, confusion and delirium). The patient suffered from cognitive impairment, emotional instability and amnesia according to her mother. There was also weakness of her left leg with gradual onset and fluctuating course. She was 106 cm tall (within normal percentile) and weighed 23.6 kg (within normal percentile), for a body mass index of 21 kg/m2. Her neurological examination revealed a focal neurologic deficit with hypotonia and hyperreflexia. Her speech showed lack of fluency and hesitation. Cranial nerves and sensory examination showed no abnormalities. About one month before, the patient was hospitalized for altered consciousness, hallucinations for which the patient had a lumbar puncture (LP) twice during her two weeks stay in hospital. The patient was given non-specific supportive treatment, except for L-thyroxin for the hypothyroid state (↓FT3, ↓FT4 and ↑TSH). Following this, the patient was discharged with no satisfactory response. There is a positive family history: The girl's mother has type 1 diabetes mellitus (T1DM) and normal thyroid profile and her aunt has Hashimoto thyroiditis that was diagnosed based on raised thyroid auto antibodies in serum, sonography andfine needle biopsy. There was a history of admission to neonatal intensive care for about 9 days and treated for possible insulin dependent diabetes. The patient's vaccinations were up to date and she was developmentally normal. The following investigations were done: complete blood count (CBC) and serum electrolytes the results of which were within normal limits; liver and kidney function tests were also normal. Erythrocyte sedimentation rate (ESR) 1st hour was 30 mm/h. Anti nuclear antibodies (ANA) and anti double stranded DNA were negative.

Other specific tests included:

Thyroid profile: Free T3 < 0.40 mmol/l (Ref. range: 0.90–300.0), Free T4 < 6.00 mmol/l (Ref. range: 5.50–140.0), and thyroid stimulating hormone (TSH) was increased to > 60.00 ulU/ml.

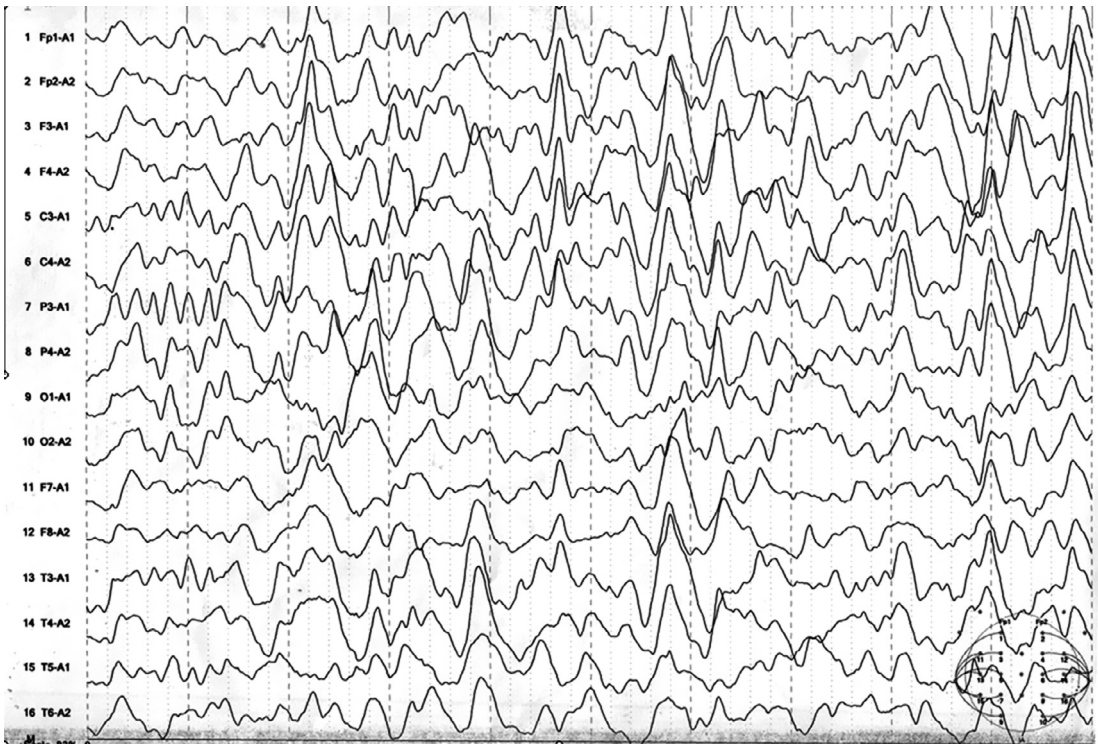

Figure 2 The first EEG evaluation done at the time of hospital admission showing slowing of background activity on an electroencephalogram.

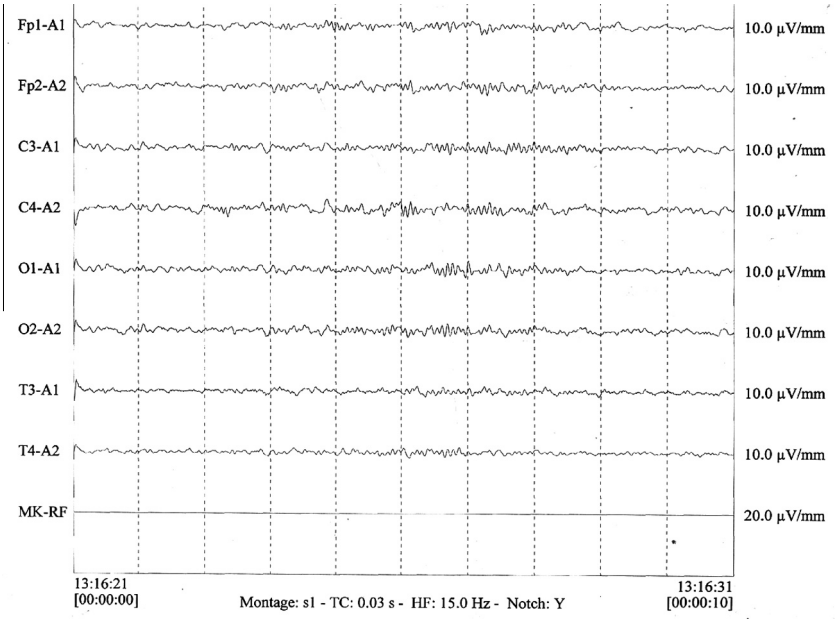

Figure 3 The second EEG evaluation done 3 weeks after clinical resolution showing a normal electroencephalogram record.

Cerebrospinal fluid (CSF) analysis: Elevated protein of 56 mg/dl (Ref. 15–45 mg/dl), glucose of 48 mg/dl (Ref. 40–70 mg/dl). Total leukocytic count (TLC) was normal and C/S was negative.

Ultrasound (U/S) on thyroid gland: Showed picture of chronic thyroiditis (hypoechogenic throid lobes), with normal size of both lobes and the isthmus (Fig. 1).

Electroencephalogram (EEG): EEG was done twice, first at the time of hospital admission, showing slowing of background activity and second 3 weeks after hospital discharge showing a normal record (Figs. 2 and 3).

Brain computerized tomography (CT): Done at the time of hospital admission, revealing unremarkable findings (Fig. 4).

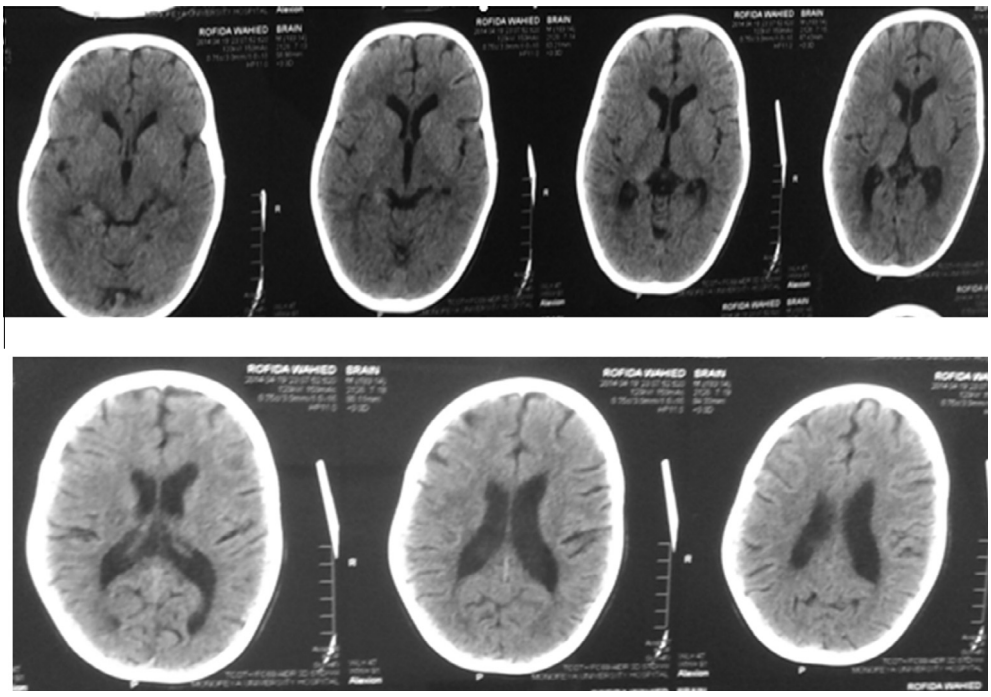

Figure 4 CT brain showing normal findings, no abnormal density.

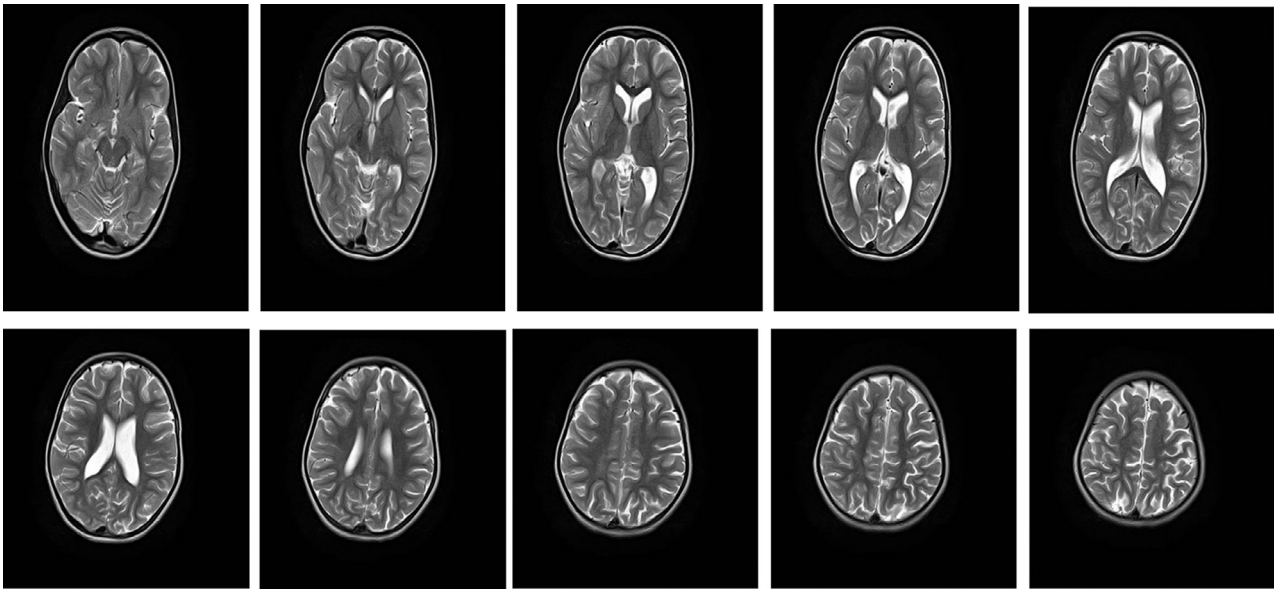

Figure 5 MRI brain showing normal findings, no abnormal density.

Brain magnetic resonance imaging (MRI): Done 2 weeks after clinical resolution of encephalopathy. It was normal; with no significant abnormal signal intensity in T2 weighted images (Fig. 5).

Autoimmune thyroid disease profiles:

Anti-thyroid antibodies: Antithyroglobulin Abs (positive) and Anti thyroid peroxidase Abs (positive), (also referred to as antimicrosomal Abs). About 2 weeks from hospital discharge, the patient. was subsequently given steroid therapy, we applied the approach which advocates a dose of oral prednisone at 60 mg/m^2/day for 10 days till now, for a total of 14 days then gradually withdrawn. Dramatic recovery was achieved, regarding good concentration, appropriate answers and satisfactory interest.

Results of our investigations are illustrated as follows:

Discussion

The term HE is now commonly used for the few hundred patients published so far. Since there is no evidence that antithyroid antibodies have a role in pathogenesis, this term

could be misleading. Some investigators proposed the term "Steroid Responsive Encephalopathy associated with Autoimmune Thyroiditis".[7] However, till the pathogenesis is under stood, the eponym "HE" seems to be the most appropriate name for the condition because it links the only known identifier, high serum concentrations of antithyroid antibodies.[8] In this case report, we discussed the importance of considering the diagnosis in the evaluation of acute or sub acute confusional state. The exact pathology of HE is unknown, but autoimmune mechanisms have been suggested because of its higher prevalence in females, fluctuating course, association with other autoimmune disorders and dramatic improvement on steroid therapy.[9]

Differential diagnosis

It is to be noted that any probable causes of encephalopathy should be ruled out such as infection, electrolyte imbalance, toxins, metabolic, degenerative causes or neoplasm. Over the last 40 years, the diagnosis of this condition has been hindered by lack of universally agreed upon diagnostic features. In response to this ambiguity, clearly defined criteria have been delineated and include encephalopathy with neurological signs, presence of antithyroid antibodies; even in the presence of the euthyroid state; and response to steroid therapy.[10] Laboratory evaluations are critical in making the diagnosis and will typically show an elevated serum level of antithyroid peroxide antibody. CSF is abnormal in approximately 80% of patients, usually revealing an elevated CSF protein level. EEG abnormalities seen in HE vary from epileptiform abnormalities, generalized slowing to normal findings.[11] Regarding brain imaging studies; In a review of 82 patients with HE, brain computed tomography or MRI showed abnormalities in 49% such as cerebral atrophy, focal cortical abnormality, diffuse subcortical abnormality and nonspecific subcortical focal white matter abnormality.[12]

The acute confusional state seen in HE is recognized as not related to the thyroid status. Correction or near correction of thyroid function abnormalities is frequently required for the diagnosis of this condition. This condition must be considered separate from confusion related to the thyroid disease since the addition of immunomodulating agents will be required for its specific treatment.[13] The long-term prognosis is variable, although a high percentage of patients respond to treatment; others could have a progressive or a relapsing course. The symptoms usually improve with glucocorticoid therapy; however, it is not necessary because of treatment. A systematic review of 85 cases published of HE found clinical response in 98% of patients treated with glucocorticoids, 92% of patients treated with glucocorticoids and levothyroxine and 67% of patients treated with levothyroxine only.[14]

HE is difficult to diagnose. Too often patients are misdiagnosed at the neurological level. It is known that if Hashimoto's encephalopathy goes untreated it results in irreversible dementia, coma, nursing home and death.

Just one person misdiagnosed is not acceptable, especially when there are so many resources available to assist proper diagnosis and appropriate treatment. The disease is not curable but treatable and with appropriate treatment, the long-term prognosis is good.[15]

Conclusion

Any patient presenting with acute or subacute unexplained encephalopathy should be considered as having HE, even if thyroid functions are normal. Thyroid antibody testing should be performed because it is the most important clue to the diagnosis. So, considering its reversible course, it is recommended that HE should be always kept in mind while evaluating disorders of the central nervous system.

N.B.: Written consent was obtained from the mother of the patient for publication of the case report and any accompanying images.

Conflict of interest

We have no conflict of interest to declare.

References

1. Erol I, Saygi S, Alehan F. Hashimoto's encephalopathy in children and adolescents. *Pediatr. Neurol.* 2011;**45**:420.
2. Nolte KW, Unbehaun A, Sieker H. Hashimoto encephalopathy: a brainstem vasculitis? *Neurology* 2000;**54**:769–70.
3. Mocellin R, Walterfang M, Velakoulis D. Hashimoto's encephalopathy: epidemiology, pathogenesis and management. *CNS Drugs* 2007;**21**:799–811.
4. Chaudhuri A, Behan PO. The clinical spectrum, diagnosis, pathogenesis and treatment of Hashimoto's encephalopathy (recurrent acute disseminated encephalomyelitis). *Curr. Med. Chem.* 2003;**10**:1945.
5. Nagpal T, Pande S. Hashimoto's encephalopathy. Response to plasma exchange. *Neurol. India* 2004;**52**:245–7.
6. Drulović J, Andrejević S, Bonaci-Nikolić B, Mijailović V. Hashimoto's encephalopathy: a long-lasting remission induced by intravenous immunoglobulins. *Vojnosanit. Pregl.* 2011;**68**:452.
7. Yu HJ, Lee J, Seo DW, Lee M. Clinical manifestations and treatment response of steroid in pediatric Hashimoto encephalopathy. *J. Child Neurol.* 2013;**29**:938.
8. Paulus W, Nolte KW. Neuropathology of Hashimoto's encephalopathy. *J. Neurol. Neurosurg. Psychiatry* 2003;**74**:1009.
9. Jenkins RC, Weetman AP. Disease associations with autoimmune thyroid disease. *Thyroid* 2002;**12**:977–88.
10. McKeon A, McNamara B, Sweeney B. Hashimoto's encephalopathy presenting with psychosis and generalized absence status. *J. Neurol.* 2004;**251**:1025.
11. Fatemi S, Bedri J, Nicoloff JT. Encephalopathy associated with Hashimoto's thyroiditis: use of serum immunoglobulin G as a marker of disease activity. *Thyroid* 2003;**13**(2):227–8.
12. v Maydell B, Kopp M, v Komorowski G, Joe A, Juengling FD. Korinthenberg R Hashimoto encephalopathy – is it underdiagnosed in pediatric patients? *Neuropediatrics* 2002;**33**(2):86–9.
13. Ferracci F, Carnevale A. The neurological disorder associated with thyroid autoimmunity. *J. Neurol.* 2006;**253**:975–84.
14. Castillo P, Woodruff B, Caselli R. Steroid – responsive encephalopathy associated with autoimmune thyroiditis. *Arch. Neurol.* 2006;**63**:197–202.
15. Taurin G, Golfier V, Pinel JF. Choreic syndrome due to Hashimoto's encephalopathy. *Mov. Disord.* 2002;**17**:1091.